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# DESCRIPTION

## EMBOLUS FORMING IN-VIVO INDWELLING COIL

### Technical Field

5       The present invention relates to an embolus forming in-vivo indwelling coil, and particularly to an embolus forming in-vivo indwelling coil used for, for example, changing or interrupting a blood flow or embolizing a lesion.

### Background Art

10       Examples of prior art document information concerning the present invention include the following:

[Patent Document 1] Patent No. 3023076

[Patent Document 2] Patent No. 2909021

[Patent Document 3] Japanese Unexamined Patent

15   Application Publication No. 8-187248

[Patent Document 4] PCT Japanese Translation Patent

Publication No. 2002-507902

[Patent Document 5] Patent No. 2908363

[Patent Document 6] Japanese Unexamined Patent

20   Application Publication No. 11-76249

      A currently known treatment with less invasive for an aneurysm or the like is vascular embolization in which an embolus forming in-vivo indwelling device is indwelled in an aneurysm. In the vascular embolization, the embolus forming  
25   in-vivo indwelling device indwelled in the aneurysm

physically interferes with a blood flow and forms a thrombus around the embolus forming in-vivo indwelling device, thereby decreasing a danger of rupture of the aneurysm. An example of the embolus forming in-vivo indwelling device  
5 which is indwelled at a predetermined position in a blood vessel, such as an aneurysm, is an embolus forming in-vivo indwelling device comprising a metal coil (referred to as an "embolus forming coil" hereinafter).

The embolus forming coil is introduced into an aneurysm  
10 through an appropriate catheter using pushing means (inductor) detachably connected to an end of the coil. Then, the embolus forming coil is separated and indwelled at the predetermined position.

However, such an embolus forming coil is required to  
15 have various characteristics: (1) In order to securely introduce and indwell the coil at the predetermined position without damaging a blood vessel, the coil has high flexibility for permitting the coil to be deformed along the shape of a blood vessel. (2) The coil has the function to  
20 prevent or suppress unrestricted stretch so as to permit a secured re-indwelling operation for recovering the coil and correcting the indwelling position after the coil has been pushed out from the catheter and placed in a blood vessel. Namely, for example, when the embolus forming coil gets  
25 caught on the tip end of the catheter and extended thereby,

the embolus forming coil cannot be easily recovered or the indwelling position may be damaged. Therefore, the embolus forming coil must be formed so as not to cause this problem.

#### Disclosure of Invention

5           The present invention has been achieved on the basis of the above-described situation, and an object of the present invention is to provide an embolus forming in-vivo indwelling coil which has so high flexibility that the coil can be securely introduced and indwelled at a predetermined  
10 position in the body, and which permits a secured re-indwelling operation including recovery of the in-vivo indwelling device, for example, for recovering the disposed device and correcting the position, and thus has high safety and high operability.

15           An embolus forming in-vivo indwelling coil of the present invention comprises a coil main body having flexibility and an stretch suppressing member which is provided on one or both of the inner and outer peripheries of the coil main body and which is made of a water-swella-  
20 ble polymer material for suppressing stretch of the coil main body by swelling with absorbed water.

          In the embolus forming in-vivo indwelling coil of the present invention, the water-swella-  
ble polymer material constituting the stretch suppressing member preferably  
25 comprises a polyvinyl alcohol polymer.

In addition, preferably, the wire constituting the coil main body has a diameter of 10 to 120  $\mu\text{m}$ , and the coil main body has a coil diameter of 100 to 500  $\mu\text{m}$ , a coil length of 2 to 500 mm, and a number of turns of 1 to 100 per unit length (1 mm).

Specifically, the rod-like or cylindrical stretch suppressing member is provided in the coil main body so as to pass through the coil main body and extend in the coil axial direction of the coil main body. In this case, the diameter of the stretch suppressing member is preferably smaller than the inner diameter of the coil main body by about 1 to 50% in a dry state.

Alternatively, the cylindrical or tubular stretch suppressing member may be provided to cover the entire region of the outer periphery of the coil main body in the coil axial direction. In this case, in a dry state, the thickness of the stretch suppressing member is preferably 0.01 to 0.10 mm, and the clearance between the outer periphery of the coil main body and the inner periphery of the stretch suppressing member is preferably 0 to 100  $\mu\text{m}$ .

The embolus forming in-vivo indwelling coil of the present invention may comprise a rod-like or cylindrical stretch suppressing member provided so as to extend in the coil axial direction of a coil main body and pass through the coil main body, and a cylindrical or tubular stretch

suppressing member provided to cover the entire region of the outer periphery of the coil main body in the coil axial direction.

5 In an indwelling operation, the embolus forming in-vivo indwelling coil of the present invention is used in a swollen state in which the stretch suppressing member is previously swollen. As a result of swelling, the stretch suppressing member enters the coil pitches (wire spaces) in the inner periphery or the outer periphery of the coil main  
10 body to create a state in which the adjacent wire turns are substantially connected to each other.

However, in the swollen state, the stretch suppressing member has deformability, and thus, basically, the flexibility of the coil main body is not significantly  
15 inhibited by the stretch suppressing member. Therefore, the embolus forming in-vivo indwelling coil can be formed with high flexibility, and high operability can be obtained in the indwelling operation. As a result, the embolus forming in-vivo indwelling coil can be securely introduced and  
20 indwelled at a predetermined position through an appropriate catheter.

Furthermore, for example, even in a re-indwelling operation for recovering the disposed coil and correcting the indwelling position, stretch of the coil main body in  
25 the coil axial direction is restricted because the wire

turns in the coil main body are substantially connected to each other by the stretch suppressing member. In this state, the embolus forming in-vivo indwelling coil is pulled back into the catheter, and thus the re-indwelling operation including recovery of the in-vivo indwelling coil can be securely performed. Therefore, the embolus forming in-vivo indwelling coil can be formed with high safety.

#### Brief Description of the Drawings

Fig. 1 is a sectional view schematically illustrating the configuration of an example of an embolus forming in-vivo indwelling coil of the present invention.

Fig. 2 is a sectional view illustrating a state in which an stretch suppressing member of the embolus forming in-vivo indwelling coil shown in Fig. 1 is swollen.

Fig. 3 is a sectional view schematically illustrating the configuration of another example of the embolus forming in-vivo indwelling coil of the present invention.

Fig. 4 is a sectional view illustrating a state in which an stretch suppressing member of the embolus forming in-vivo indwelling coil shown in Fig. 3 is swollen.

Fig. 5 is an enlarged sectional view illustrating the configuration of still another example of the embolus forming in-vivo indwelling coil of the present invention.

Fig. 6 is an enlarged sectional view illustrating the configuration of a further example of the embolus forming

in-vivo indwelling coil of the present invention.

Fig. 7 is a drawing illustrating a method for measuring the flexibility of an in-vivo indwelling device according to the present invention.

5 Best Mode for Carrying Out the Invention

The present invention will be described in detail below with reference to the drawings.

Fig. 1 is a sectional view schematically illustrating the configuration of an example of an embolus forming in-  
10 vivo indwelling coil of the present invention.

The embolus forming in-vivo indwelling coil (simply referred to as an "in-vivo indwelling coil" hereinafter) 10 comprises a coil main body 11 having flexibility. Also, for example, a rod-shaped coil separating member 12 for holding  
15 the coil main body 11 is provided at the proximal end (the right-side end in Fig. 1) of the coil main body 11 so as to be partially fixed on the inner periphery of the coil main body 11 at the proximal end to project outward (rightward in Fig. 1) from the proximal end of the coil main body 11 in  
20 the coil axial direction.

As a wire for the coil main body 11, any one of various materials, for example, a metal wire, a resin wire, and the like, can be used as long as the wire does not adversely affect a human body (having biocompatibility) when being  
25 indwelled in the human body for a long time.

Examples of the metal wire for forming the coil main body 11 include tungsten, gold, platinum, and stainless steel, and alloys thereof.

5 Examples of the resin wire include polyester resins such as polyethylene terephthalate (PET), polyolefin resins such as polypropylene (PP), and polyamide resins such as nylon.

As described above, the coil main body 11 constituting the in-vivo indwelling coil 10 has flexibility and  
10 preferably has the structure below depending upon the material of the wire used for forming the coil main body 11.

For example, the diameter (element wire diameter) of the wire constituting the coil main body 11 is 10 to 120  $\mu\text{m}$ , and the coil main body 11 has a coil diameter of 100 to 500  
15  $\mu\text{m}$ , a coil length of 2 to 500 mm, and a number of turns of 1 to 100 per unit length (1 mm).

The in-vivo indwelling coil 10 further comprises an stretch suppressing member 15 of, for example, a rod shape, which is made of a water-swellaable polymer material and  
20 functions to suppress stretch of the coil main body 11 by swelling with absorbed water, and which is provided to extend in the coil axial direction of the coil main body 11 and to pass through the coil main body 11 (through a lumen).

As the polymer material constituting the stretch  
25 suppressing member 15, any material which has proper water-



swellability and no adverse effect on human bodies can be used. Specific examples of the polymer material include polyvinyl alcohol polymers; natural polysaccharides such as carrageenan, agar, alginic acid, starch, pectin,  
5 galactomannan, xanthane, hyaluronic acid, chitin, and chitosan; natural proteins such as collagen, actin, myosin, tublin, casein, and fibrin; chemically-modified natural polymers such as carboxymethylated cellulose, carboxymethylated starch, acrylic acid-grafted starch,  
10 acrylonitrile-grafted cellulose hydrolyzates; and synthetic polymers such as polyacrylic acid, polyvinyl alcohol, polyethyleneimine, polyhydroxyethyl methacrylate, polyvinylpyrrolidone, and polyethylene oxide. Among these materials, polyvinyl alcohol polymers are preferred because  
15 a crystalline substance can be easily oriented, and excellent physical strength can be achieved by orienting a crystalline substance.

The diameter of the stretch suppressing member 15 depends on the water-swellability of the material of the  
20 stretch suppressing member 15, but the diameter may be determined so that in a dry state, it can be inserted into the coil main body (lumen). For example, the diameter is preferably smaller than the coil diameter of the coil main body 11 by about 1 to 50%.

25 From the viewpoint that a desired stretch preventing

effect is securely expressed in a swollen state, the stretch suppressing member 15 is preferably disposed to extend over the entire region of the coil main body 11 in the coil axial direction. In other words, the stretch suppressing member 5 15 preferably has a length which is the same as or larger than the coil length of the coil main body 11.

As shown in Fig. 3, in the in-vivo indwelling coil 10 of the present invention, for example, the cylindrical or tubular stretch suppressing member 15 may be provided to 10 cover the entire region of the outer periphery of the coil main body 11 in the coil axial direction.

The thickness of the stretch suppressing member 15, which constitutes the in-vivo indwelling coil 10, can be properly determined to express the intended stretch 15 preventing effect in a swollen state. Specifically, in a dry state, the diameter is preferably 0.01 to 0.10 mm, and the clearance between the outer periphery of the coil main body 11 and the inner periphery of the stretch suppressing member 15 is preferably 0 to 100  $\mu\text{m}$ .

20 The above-described in-vivo indwelling coil 10 can be also used in a state in which the linear primary form is maintained. However, in view of improvement in the embolus forming ability at a predetermined position, the coil 10 is preferably used, for example, in a state in which the linear 25 coil main body 11 is helically coiled to form a secondary

coil or in a state in which the coil main body 11 is formed in a S- or J-like three-dimensional shape, or another secondary shape.

5 The method for using the in-vivo indwelling coil 10 will be described below with reference to an example in which the coil 10 is applied to treatment of an aneurysm.

First, the stretch suppressing member 15 constituting the in-vivo indwelling coil 10 is swollen by, for example, immersing in appropriate swelling water.

10 The swelling water is not particularly limited as long as it is not harmful to organisms. For example, physiological saline, purified water, extra-pure water, ion-exchanged water, an aqueous solution of a compound such as dimethylsulfoxide, blood, or the like can be used.

15 In swelling the stretch suppressing member 15, the time of immersion of the in-vivo indwelling coil 10 in the swelling water is preferably, for example, 5 to 180 seconds depending on the constitutive material and configuration of the stretch suppressing member 15, and the like.

20 When the stretch suppressing member 15 of the in-vivo indwelling coil 10 is swollen, the stretch suppressing member 15 enters the coil pitches (wire spaces) in the inner periphery of the coil main body 11 as shown in Fig. 2, or the stretch suppressing member 15 enters the coil pitches in  
25 the outer periphery of the coil main body 11 as shown in Fig.

4. Namely, the adjacent turns of the wire, which constitutes the coil main body 11, are substantially connected to each other. In this state, the indwelling coil 10 is formed in a secondary shape, for example, a secondary coil, and then detachably mounted on the tip of a guide wire.

Examples of a method for separating the in-vivo indwelling coil 10 from the guide wire include a mechanical separating method (1) in which the coil separating member 12 of the in-vivo indwelling coil 10 is mechanically engaged with the guide wire, and an electric separating method (2) in which for example, a monopolar high-frequency current is supplied to melt and disconnect the coil separating member 12 of the in-vivo indwelling coil 10 by heating with the high-frequency current, thereby separating the in-vivo indwelling coil 10 from the guide wire.

Then, a proper catheter is endermically inserted into a blood vessel using a puncture needle until the end of the catheter reaches the inlet of an aneurysm. Thereafter, the in-vivo indwelling coil 10 is linearly stretched and returned to the primary form (shown in Fig. 2 or 4). In this state, the guide wire is inserted into the catheter and moved forward to push out the in-vivo indwelling coil 10 from the end of the catheter and dispose the in-vivo indwelling coil 10 in the aneurysm.

When the in-vivo indwelling coil 10 is push out from

the catheter, it is restored to the secondary coil, which is a secondary form, in which the in-vivo indwelling coil 10 is three-dimensionally tangled. In this state, the complete insertion of the in-vivo indwelling coil 10 into the

5 aneurysm is confirmed by radioscopy. Then, the in-vivo indwelling coil 10 is separated from the end of the guide wire and indwelled in the aneurysm.

If required, the above-described indwelling operation is repeated using a plurality of the in-vivo indwelling  
10 coils 10 to fill the aneurysm with a plurality of in-vivo indwelling coils 10 and form a thrombus, thereby inhibiting a blood inflow to the aneurysm. As a result, rupture of the aneurysm can be securely prevented.

In the indwelling operation, the in-vivo indwelling  
15 coil 10 of the present invention is used after the stretch suppressing member 15 is previously swollen. When the stretch suppressing member 15 is swollen, therefore, the stretch suppressing member 15 enters the wire spaces in the inner periphery or the outer periphery of the coil main body  
20 11 to create a state in which the adjacent wire turns are substantially connected to each other.

Specifically, in the in-vivo indwelling coil 10 having the structure shown in Fig. 1, the stretch suppressing member 15 is swollen to fill in the coil main body 11  
25 (lumen) and enters the coil pitches in the inner periphery

of the coil main body 11, as shown in Fig. 2. In the in-vivo indwelling coil 10 having the structure shown in Fig. 3, the stretch suppressing member 15 is swollen to enter the coil pitches from the outer periphery of the coil main body 11, thereby causing a state in which the adjacent wire turns are substantially connected to each other. As a result, the coil main body 11 is supported by the stretch suppressing member 15.

Therefore, the stretch suppressing member 15 is formed with deformability in a swollen state, and thus, basically, the flexibility of the coil main body 11 is not significantly inhibited by the stretch suppressing member 15. Therefore, the in-vivo indwelling coil 10 can be formed with high flexibility, and high operability of the indwelling operation can be achieved. Consequently, the in-vivo indwelling coil 10 can be securely introduced and indwelled at the predetermined position through the appropriate catheter.

Furthermore, when a re-indwelling operation is required for recovering the disposed coil and correcting the indwelling position, the in-vivo indwelling coil 10 of the present invention is returned into the catheter in the state in which stretch of the coil main body in the coil axial direction is restricted because the adjacent turns of the wire constituting the coil main body 11 are substantially

connected to each other by the stretch suppressing member 15. Therefore, the re-indwelling operation including recovery of the in-vivo indwelling coil 10 can be securely performed.

As a result, the in-vivo indwelling coil 10 can be formed

5 with high safety.

In the in-vivo indwelling coil having the structure shown in Fig. 3, the stretch suppressing member 15 is provided over the entire region of the outer periphery of the coil main body 11, and the stretch suppressing member 15

10 is made of a flexible material having deformability in a swollen state. Therefore, the lubricating effect is exhibited in moving the in-vivo indwelling coil 10 inserted in the catheter to the predetermined position, thereby achieving high operability. Also, since the coil main  
15 body 11 is not exposed, damage to the applied position can be securely prevented to achieve the function to protect the applied position.

The preferred embodiments of the present invention are described above, but the present invention is not limited to  
20 these embodiments, and the modifications below can be made.

(1) An stretch suppressing member may be disposed so as to realize a state in which in a swollen state, the stretch suppressing member enters the spaces of a wire constituting a coil main body. For example, as shown in Fig. 5, the  
25 stretch suppressing member may be formed into a film so as

to cover the entire surface of the wire in a dry state and connect the adjacent wire turns. Alternatively, as shown in Fig. 6, the stretch suppressing member may be formed into a film so as to fill in wire spaces in a dry state. In these  
5 structures, the stretch suppressing member is put into a flexible state with deformability when being swollen, and thus stretch of the coil main body can be securely restricted by the stretch suppressing member without significantly inhibiting the flexibility of the coil main  
10 body.

In the in-vivo indwelling coil shown in Fig. 1, the stretch suppressing member may be formed, for example, in a cylindrical shape. In this case, the specific structural conditions of the stretch suppressing member, such as the  
15 thickness and the outer diameter dimension thereof, and the like, may be properly determined so that the intended stretch suppressing function can be exhibited.

(2) Although not shown in a drawing, the in-vivo indwelling coil of the present invention may comprise an  
20 internal stretch suppressing member inserted into a coil main body and an external stretch suppressing member provided to cover the entire surface of the outer periphery of the coil main body. In this case, the internal and external stretch suppressing members are swollen to enter  
25 the coil pitches in the coil main body from both the inner



side and the outer side, thereby forming a state in which the adjacent wire turns can be substantially connected to each other. Therefore, a higher stretch suppressing effect on the coil main body can be obtained. When the internal stretch suppressing member is formed in, for example, a cylindrical shape, the intended stretch suppressing effect can be securely exhibited without significantly increasing the time required for swelling.

(3) A coil main body may comprise a fiber material, for example, polyester or the like, which is woven into a loop and provided on the coil main body, or a fiber material woven into a cylindrical form to cover the outer surface of the coil main body. In this case, the in-vivo indwelling coil can be formed with a higher embolus forming ability.

#### <Experimental Example>

The experimental examples conducted for confirming the functional effect of the in-vivo indwelling coil of the present invention will be described below.

#### [Production Example 1]

A rod-shaped stretch suppressing member comprising polyvinyl alcohol and having a diameter of 120  $\mu\text{m}$  and a length of 50 mm was inserted into a metal coil (coil diameter: 250  $\mu\text{m}$ , coil length: 50 mm, number of turns per 1 mm: 20) which was formed by coiling a tungsten wire having an element wire diameter of 50  $\mu\text{m}$ . As a result, an in-vivo

indwelling coil having the structure shown in Fig. 1 was produced. This is referred to as "indwelling coil 1".

[Production Example 2]

A metal coil having the same structure as in Production  
5 Example 1 was formed, and a cylindrical stretch suppressing  
member comprising polyvinyl alcohol and having a diameter of  
350  $\mu\text{m}$ , a thickness of 50  $\mu\text{m}$ , and a length of 50 mm was  
disposed to cover the entire region of the outer periphery  
of the metal coil to produce an in-vivo indwelling coil  
10 having the structure shown in Fig. 3. This is referred to  
as "indwelling coil 2".

[Production Example 3]

A metal coil having the same structure as in Production  
Example 1 was formed, and a rod-shaped stretch suppressing  
15 member comprising polyvinyl alcohol and having a diameter of  
120  $\mu\text{m}$  and a length of 50 mm was inserted into the metal  
coil. Furthermore, a cylindrical stretch suppressing member  
comprising polyvinyl alcohol and having a diameter of 350  $\mu\text{m}$ ,  
a thickness of 50  $\mu\text{m}$ , and a length of 50 mm was disposed to  
20 cover the entire region of the outer periphery of the metal  
coil was disposed to cover the entire region of the outer  
periphery of the metal coil to produce an in-vivo indwelling  
coil. This is referred to as "indwelling coil 3".

Each of the indwelling coils 1 to 3 produced as  
25 described above was subjected to swelling of the stretch

suppressing member under the conditions shown in Table 1,  
and then evaluated with respect to (1) flexibility of the  
whole indwelling coil and (2) the stretch suppressing  
function of the stretch suppressing member on the coil main  
5 body in a swollen state. The results are shown in Table 1.  
[Evaluation]

(1) The flexibility of the whole indwelling coil was  
determined as follows:

As shown in Fig. 7, the in-vivo indwelling coil 10 was  
10 fixed with a tube so that the primary coil axis of the coil  
main body 11 was extended in, for example, the vertical  
direction (the longitudinal direction in Fig. 7). In a  
state in which any portion in the range from half pitch to  
one pitch of a secondary coil was exposed, a load was slowly  
15 applied to the in-vivo indwelling coil 10 from above in the  
coil axial direction, and the stress produced when the  
portion in the range from half pitch to one pitch was bent  
at the end of the coil main body 11 was measured as  
compressive elasticity modulus. In Fig. 7, reference  
20 numeral 13 denotes the rounded head having a substantially  
hemispherical shape and provided at the distal end of the  
in-vivo indwelling coil 10.

(2) Each of the indwelling coils subjected to swelling  
was measured with respect to the coil length of the coil  
25 main body when a load of  $80 \text{ mN/mm}^2$  was applied outward in

the coil axial direction of the coil main body, and an elongation of the coil main body was calculated.

Table 1

	Swelling conditions		Flexibility of whole indwelling coil (mN/mm <sup>2</sup> )	Elongation of coil main body (mm)
	Swelling water	Rate of volume increase (%)		
Indwelling coil 1	Purified water	185	8	3
Indwelling coil 2	Physio- logical saline	115	8	3
Indwelling coil 3	Purified water	123	10	2

5           The results confirm that in the indwelling coils 1 to 3  
of the present invention, the elongation of the coil main  
body in the coil axial direction is restricted to 3 mm or  
less, and the intended stretch suppressing effect is  
securely exhibited, and that the in-vivo indwelling coils  
10 have high flexibility. Therefore, it can be expected that  
high operability and high safety are obtained in an  
indwelling operation, and the indwelling operation can be  
reliably performed.

#### Industrial Applicability

15           In an indwelling operation, an embolus forming in-vivo  
indwelling coil of the present invention is used in a state  
in which a stretch suppressing member is previously swollen.

As a result of swelling, the stretch suppressing member enters the coil pitches (wire spaces) in the inner periphery or the outer periphery of the coil main body to create a state in which the adjacent wire turns are substantially  
5 connected to each other.

However, in the swollen state, the stretch suppressing member has deformability, and thus, basically, the flexibility of the coil main body is not significantly inhibited by the stretch suppressing member. Therefore, the  
10 embolus forming in-vivo indwelling coil can be formed with high flexibility, and high operability can be obtained in the indwelling operation. As a result, the embolus forming in-vivo indwelling coil can be securely introduced and indwelled at a predetermined position through an appropriate  
15 catheter.

Furthermore, for example, even in a re-indwelling operation for recovering the disposed coil and correcting the indwelling position, stretch of the coil main body in the coil axial direction is restricted because the wire  
20 turns in the coil main body are substantially connected to each other by the stretch suppressing member. In this state, the embolus forming in-vivo indwelling coil is pulled back into the catheter, and thus the re-indwelling operation including recovery of the in-vivo indwelling coil can be  
25 securely performed. Therefore, the embolus forming in-vivo

indwelling coil can be formed with high safety.